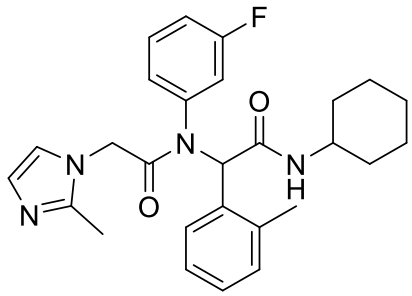
Product data sheet

MedKoo Cat#: 406264 Name: AGI-5198 CAS#: 1355326-35-0 Chemical Formula: $C_{27}H_{31}FN_4O_2$ Exact Mass: 462.2431 Molecular Weight: 462.55904	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
AGI-5198, also know as IDH-C35, is the a very potent and selective mutant IDH1 inhibitor that was shown to potential anticancer activity. AGI-5198 shows good potency in the U87 R132H cell based assay and ~90% tumor 2-HG inhibition in the corresponding mouse xenograft model following BID dosing. AGI-5198 inhibits IDH1 R132H mutant and R132C mutant in vitro with IC50 ~0.07 μM and ~0.16 μM, respectively.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	24	51.89
Ethanol	14	30.27

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.16 mL	10.81 mL	21.62 mL
5 mM	0.43 mL	2.16 mL	4.32 mL
10 mM	0.22 mL	1.08 mL	2.16 mL
50 mM	0.04 mL	0.22 mL	0.43 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Rohle D, Popovici-Muller J, Palaskas N, Turcan S, Grommes C, Campos C, Tsoi J, Clark O, Oldrini B, Komisopoulou E, Kunii K, Pedraza A, Schalm S, Silverman L, Miller A, Wang F, Yang H, Chen Y, Kernytsky A, Rosenblum MK, Liu W, Biller SA, Su SM, Brennan CW, Chan TA, Graeber TG, Yen KE, Mellinghoff IK. An inhibitor of mutant IDH1 delays growth and promotes differentiation of glioma cells. Science. 2013 May 3;340(6132):626-30. doi: 10.1126/science.1236062. Epub 2013 Apr 4. PMID: 23558169; PMCID: PMC3985613.

In vivo study

1. Rohle D, Popovici-Muller J, Palaskas N, Turcan S, Grommes C, Campos C, Tsoi J, Clark O, Oldrini B, Komisopoulou E, Kunii K, Pedraza A, Schalm S, Silverman L, Miller A, Wang F, Yang H, Chen Y, Kernytsky A, Rosenblum MK, Liu W, Biller SA, Su SM, Brennan CW, Chan TA, Graeber TG, Yen KE, Mellinghoff IK. An inhibitor of mutant IDH1 delays growth and promotes differentiation of glioma cells. Science. 2013 May 3;340(6132):626-30. doi: 10.1126/science.1236062. Epub 2013 Apr 4. PMID: 23558169; PMCID: PMC3985613.

7. Bioactivity

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Biological target:

AGI-5198 (IDH-C35) is a potent and selective mutant IDH1R132H inhibitor with an IC50 of 0.07 μM.

In vitro activity

The activity of AGI-5198 in TS603 glioma cells with an endogenous heterozygous R132H-IDH1 mutation, the most common IDH mutation in glioma, was explored. TS603 cells were derived from a patient with anaplastic oligodendroglioma (WHO grade III) and harbor another pathognomomic lesion for this glioma subtype, namely co-deletion of the short arm of chromosome 1 (1p) and the long arm of chromosome 19 (19q) (19) (Fig. 1C). Measurements of R-2HG concentrations in pellets of TS603 glioma cells demonstrated dose-dependent inhibition of the mutant IDH1 enzyme by AGI-5198 (Fig. 1D). When added to TS603 glioma cells growing in soft agar, AGI-5198 inhibited colony formation by 40 to 60% (Fig. 1E). AGI-5198 did not impair colony formation of two patient-derived glioma lines that express only the wild-type IDH1 allele (TS676 and TS516) (Fig. 1F), further supporting the selectivity of AGI-5198.

Reference: Science. 2013 May 3;340(6132):626-30. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/23558169/

In vivo activity

The effects of orally administered AGI-5198 on the growth of human glioma xenografts were examined. When given daily to mice with established R132H-IDH1 glioma xenografts, AGI-5198 [450 mg per kg of weight (mg/kg) per os] caused 50 to 60% growth inhibition (Fig. 2A). Treatment was tolerated well with no signs of toxicity during 3 weeks of daily treatment (fig. S3). Tumors from AGI-5198– treated mice showed reduced staining with an antibody against the Ki-67 protein, a marker used for quantification of tumor cell proliferation in human brain tumors. In contrast, staining with an antibody against cleaved caspase-3 showed no differences between tumors from vehicle and AGI-5198–treated mice (fig. S4), suggesting that the growth-inhibitory effects of AGI-5198 were primarily due to impaired tumor cell proliferation rather than induction of apoptotic cell death. AGI-5198 did not affect the growth of IDH1 wild-type glioma xenografts (Fig. 2B).

Reference: Science. 2013 May 3;340(6132):626-30. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/23558169/